PSJ17 Exh 11

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-947/S-005

COMPLETE RESPONSE

Cephalon, Inc
c/o CIMA Labs
41 Moores Road
P.O. Box 4011
Frazer, PA 19355

Attention: Penny Levin, M.S.
Director, Regulatory Affairs

Dear Ms. Levin:

Please refer to your supplemental New Drug Application (sNDA) dated November 9, 2007, received November 13, 2007, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Fentora (fentanyl buccal tablets).

We acknowledge receipt of your amendments dated January 3, 7, and 28, February 11, March 5, 11, 20, 25, 27 (2), and 28, and April 3, and 9, 2008.

This supplemental new drug application provides for the use of Fentora for the management of breakthrough pain in patients who are already regularly taking around-the-clock opioid medicine for their underlying persistent pain.

We have completed the review of your application, as amended, and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues.

CLINICAL

Although your application provides evidence to support the efficacy and safety of Fentora for use in the expanded non-cancer breakthrough pain population, you have not adequately addressed the public health concern of increased abuse, misuse, overdose and addiction that is to be expected with more widespread availability of this product in the community. Your proposed plan to mitigate these risks has not been adequately tested to assure that it will, indeed, achieve this outcome for your currently approved indication, let alone the proposed expanded indication. In the face of a national crisis of prescription opioid abuse and misuse, it is critical that you provide a risk management program with established efficacy, adequate restrictions to avoid widespread abuse and misuse, and adequate flexibility to assure access for legitimate patients, before this expanded indication can be approved.

We reserve comment on the proposed labeling until the application is otherwise adequate. If you revise labeling, your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(*b*). The safety update should include data from all nonclinical and clinical studies/trials of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.

2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

   a. Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.

   b. Present tabulations of the new safety data combined with the original NDA data.

   c. Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.

   d. For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.

4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.

5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.

6. Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).

7. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.

8. Provide English translations of current approved foreign labeling not previously submitted.

OTHER

Within one year after the date of this letter, you are required to resubmit or take one of the other actions available under 21 CFR 314.110. If you do not take one of these actions, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA Guidance for Industry *Formal Meetings With Sponsors and Applicants for PDUFA Products*, February, 2000 (http://www.fda.gov/cder/guidance/2125fnl.htm).

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with this change before approval of this supplemental application.

If you have any questions, call Kimberly Compton, R.Ph., Regulatory Project Manager, at (301) 796-1191.

Sincerely,

{See appended electronic signature page}

Bob A. Rappaport, M.D.
Director
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center of Drug Evaluation and Research

This is a r presentation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Bob Rappaport
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